UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,539	05/01/2001	Lars Bjorck	100084.415US	4148

7590 09/24/2003

David Kalow
Kalow & Springut LLP
488 Madison Avenue 19th Floor
New York, NY 10022

EXAMINER	
BASKAR, PADMAVATHI	

ART UNIT	PAPER NUMBER
1645	19

DATE MAILED: 09/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/847,539	Applicant(s) BJORCK ET AL.	
	Examiner Padmavathi v Baskar	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23 and 25 – 38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23 and 25 – 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to Amendment

1. Applicant's amendment filed on 6/23/03 (Paper # 17) is acknowledged. Claims 24 and 39 have been canceled. Claims 23, 25 and 29 ~~has~~ have been amended. Claims 23, 25-38 are under examination.

Priority

2. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)(d) to application United Kingdom 9823975.9. The certified copy of United Kingdom 9823975.9 has been received and foreign priority has been accorded as of the filing date of the priority document, 11/2/1998.

3. The examiner acknowledges the new title and has been placed in the application.

Rejection Withdrawn

4. In view of amendment to the claims, the rejection of claims 23 and 25 -38 under 35 U.S.C. 101 non-statutory subject matter is withdrawn.

Rejections Maintained

5. The rejection of claims 23, 25-38 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated protein that is capable of binding to α_2 M that comprises the amino acid sequence of SEQ.ID.NO: 6 does not reasonably provide enablement for a functional variant thereof that is capable of binding to α_2 M and has at least 78% homology to amino acids to SEQ.ID.NO: 6 over at least 30 amino acids or over at least 100 amino acids or a variant with at least 75% homology to amino acids 59 to 86 of SEQ.ID.NO: 6 or a peptide fragment comprising 6, 15 and 20 amino acids of SEQ.ID.NO: 6 or variants with at least 75%

and 78% homology to amino acids 59 to 86 of SEQ.ID.NO: 6 or functional variant comprising one or more tandem repeats is maintained as set forth in the previous office action.

The specification is not enabled for a functional variant thereof or functional variant with 75% and 78% homology to amino acids 59 to 86 of SEQ.ID.NO: 6 or peptide fragments comprising 6, 15 and 20 amino acids of SEQ.ID.NO: 6 or variants with at least 75% and 78% homology to amino acids 59 to 86 of SEQ.ID.NO: 6 because the specification is totally silent. If it is unclear to one skilled in the art what are those functional equivalents or sequences are embraced by the claim since the specification lacks the algorithm and parameters used to determine percent identity or derivatives of fragments.

The specification is silent in what changes have been made to SEQ.ID.NO: 6 to obtain the above functional variants. It is well known that for proteins, for example, even a single amino acid change can destroy the function of the biomolecule. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Further, specification is silent on how to make these proteins with sequence homology or variants or fragments. What changes would have an adverse effect on the function of this peptide is not predictable. It is known in the art that derivatives or variants, which are obtained by substitutions, deletions, or modifications of the amino acids of a protein, alter the function of th protein. The amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and still retain similar activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expected intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, the problem of predicting protein structure from mere sequence data of a single protein and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex (Bowie et al. Science, Vol. 247: 1990; p. 1306; p. 1308) and is well outside the realm of routine experimentation.

Applicant's arguments filed on 6/23/03 have been fully considered but they are not deemed to be persuasive.

Applicant states that in light of the amendments made to the claims, the rejection under 35 U.S.C. 112, first paragraph is inappropriate, variant as described in page 6, lines 4-6 can be used in vaccine formulation for generating preferably a protective immune response, procedures identifying candidates for generating an immune response have been illustrated in page 11, lines 14-21 and pages 7 and 14 teach calculating homology and amino acid identity and therefore, the rejection should be withdrawn.

The xaminer has reviewed the citations which applicant pointed to the examiner and found no support for the claimed language. While specification teaches general m thods of calculating homology but does not teach how to make and use the variants as claimed in the specification. The variants, which bind to α 2 macroglobulin, have not been taught by the specification. The state of the art teaches (see IDS, AQ reference, first two paragraphs) that the interaction between streptococci and the two forms of α_2 macroglobulin (α_2 M) is highly specific. While human pathogenic streptococci bind to native form of α_2 M, bovine and equine streptococci interact with proteinase complexed form of α_2 M. Therefore, the amino acid sequence of a protein determines its structural and functional properties such as binding to the α_2 M. What changes can be tolerated in a protein to retain its functional activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved, and detailed knowledge of the ways in which the proteins' structure relates to its function have not been disclosed with regard to variants. However, the problem of predicting protein structure from mere sequence data of a single protein and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex (Bowie et al. Science, Vol. 247: 1990; p. 1306; p. 1308) and is well outside the realm of routine experimentation.

7. The rejection of claims 23 and 25 – 38 under 35 U.S.C. 102(b) as being anticipated by Lammler et al 1986 (Zbl.Bakt.Hyg A 261, 161-166) is maintained as set forth in the previous office action.

Lammler et al disclose ten of the 11 streptococcal cultures of serological group A, T type 4 possessing antigen (T4) bound to α_2 macroglobulin (see abstract, Table 1). Further, the prior art disclose that only on strain 71-715 did not bind to α_2 macroglobulin but other 10 strains including S.pyogenes strain 71-727 bound to α_2 macroglobulin (see page 163 under binding of

plasma proteins). Thus the prior art reads on claim 28 as well. In the absence of evidence to the contrary the disclosed prior art streptococcal proteins comprise amino acid sequence of SEQ.ID.NO: 6. Since the Office does not have the facilities for examining and comparing applicants' claimed protein with the T4 antigen of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed protein and the T 4 antigen of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Applicant's arguments filed on 6/23/03 have been fully considered but they are not deemed to be persuasive.

Applicant states that the cited reference did not disclose the sequence, SEQ.ID.NO: 6 or variant.

The examiner has rejected the claims based on inherency. Protein T4 (antigen) bound to the α_2 macroglobulin and therefore, it contains the amino acid sequence SEQ.ID.NO: 6. Applicant did not show any evidence that the disclosed protein and the claimed invention are not the same.

8. The rejection of claims 23 and 25 – 38 under 35 U.S.C. 102(b) as being anticipated by Chhatwal et al (J.Bacteriology, 169; 3691-3695) is maintained as set forth in the previous office action.

Chhatwal et al disclose streptococcal cultures of serological group A, including S.pyogenes strain A8189 bound to α_2 macroglobulin (see abstract, Table 1 and figure 3). Further, the prior art disclose streptococcal lysates and purified proteins bind to α_2 macroglobulin as well as antibodies to α_2 macroglobulin indicating that the protein binds to α_2 macroglobulin (see figure 4). S.pyogenes strain A8189 bound to α_2 macroglobulin (figures 1-4) since this strain is not SF 370, would read on claim 28. In the absence of evidence to the contrary the disclosed prior art streptococcal protein (α_2 M-binding protein) comprise amino acid sequence of SEQ.ID.NO: 6. Since the Office does not have the facilities for examining and comparing applicants' claimed protein with th protein of the prior art, the burden is on applicant to show a novel or unobvious differenc between the claimed protein and the protein of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Applicant's arguments filed on 6/23/03 have been fully considered but they are not deemed to be persuasive.

Applicant states that the cited reference did not disclose the sequence, SEQ.ID.NO: 6 or variant.

The examiner has rejected the claims based on inherency since streptococcal protein (α_2 M-binding protein) bound to the α_2 macroglobulin and therefore, it contains the amino acid sequence SEQ.ID.NO: 6. Applicant did not show any evidence that the disclosed protein and the claimed invention are not the same.

Status of Claims

9. No claims are allowed.

Conclusion

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will th statutory period for response expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be r ached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D.

9/16/03

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600